2018 Current Fiscal Year Report: Pharmacy Compounding Advisory Committee

Report Run Date: 06/05/2019 12:30:09 PM

1. Department or Agency	2. Fiscal Year
Department of Health and Human Services	2018

3. Committee or Subcommittee	3b. GSA Committee No.
Pharmacy Compounding Advisory Committee	5220

4. Is this New During Fiscal Year?	5. Current Charter	6. Expected Renewal Date	7. Expected Term Date
No	04/25/2018	04/25/2020	

8a. Was Terminated During FiscalYear?	8b. Specific Termination Authority	8c. Actual Term Date
No		

9. Agency Recommendation for Next FiscalYear	10a. Legislation Req to Terminate?	10b. Legislation Pending?
Continue	Not Applicable	Not Applicable

11. Establishment Authority Statutory (Congress Created)

12. Specific Establishment Authority	13. Effective Date	14. Commitee Type	14c. Presidential?
21 U.S.C. 353a	11/21/1998	Continuing	No

15. Description of Committee Scientific Technical Program Advisory Board

16a. Total Number of Reports	No Reports for this FiscalYear

17a. Open 2 **17b. Closed** 0 **17c. Partially Closed** 0 **Other Activities** 0 **17d. Total** 2

Meetings and Dates

Purpose	Start	End
During the morning session on November 20, 2017, the committee discussed three bulk drug substances nominated for inclusion on the list of bulk drug substances that can be used to compound drug products in accordance with section 503A of the FD&C Act: astragalus, L-citrulline, and pregnenolone. During the afternoon session on November 20, 2017, the committee discussed three additional bulk drug substances nominated for inclusion on the list of bulk drug substances that can be used to compound drug products in accordance with section 503A of the FD&C Act: 7-keto dehydroepiandrosterone (7-keto DHEA), epigallocatechin gallate (EGCg), and resveratrol. On November 21, 2017, the committee discussed the following drug products, which were nominated as drug products that present demonstrable difficulties for compounding and that cannot be compounded under sections 503A and 503B of the FD&C Act: liposome drug products and drug products produced using hot melt extrusion.	11/20/2017	11/21/2017
The committee received information on the following two issues to follow up on discussions from previous PCAC meetings: balancing the criteria for the 503A bulk drug substance evaluation and compounding as it relates to dietary supplements. In addition, the committee discussed five bulk drug substances nominated for inclusion on the 503A Bulks List. FDA discussed the following nominated bulk drug substances: Alpha lipoic acid, coenzyme Q10, creatine monohydrate, pyridoxal 5 phosphate, and quercetin dihydrate.	09/12/2018	09/12/2018

Number of Committee Meetings Listed: 2

	Current FY	Next FY
18a(1). Personnel Pmts to Non-Federal Members	$21,191.00	$15,312.00
18a(2). Personnel Pmts to Federal Members	$0.00	$0.00
18a(3). Personnel Pmts to Federal Staff	$141,017.00	$139,750.00
18a(4). Personnel Pmts to Non-Member Consultants	$3,143.00	$5,468.00
18b(1). Travel and Per Diem to Non-Federal Members	$16,486.00	$10,774.00
18b(2). Travel and Per Diem to Federal Members	$0.00	$0.00
18b(3). Travel and Per Diem to Federal Staff	$0.00	$0.00
18b(4). Travel and Per Diem to Non-member Consultants	$1,661.00	$2,086.00
18c. Other(rents,user charges, graphics, printing, mail, etc.)	$40,344.00	$38,365.00
18d. Total	$223,842.00	$211,755.00
19. Federal Staff Support Years (FTE)	1.10	1.10

20a. How does the Committee accomplish its purpose?

The Committee provides advice on scientific, technical, and medical issues concerning drug compounding under sections 503A and 503B of the Federal Food, Drug, and Cosmetic Act, and, as required, any other product for which the Food and Drug Administration has regulatory responsibility, and make appropriate recommendations to the Commissioner of Food and Drugs.

20b. How does the Committee balance its membership?

Members are authorities in the fields of pharmacy compounding, pharmaceutical manufacturing, pharmacy, medicine, and related specialties. The core of voting members may include one or more technically qualified members, selected by the Commissioner or designee, who are identified with consumer interests and are recommended by either a consortium of consumer-oriented organizations or other interested persons. In addition to the voting members, the Committee may include one or more non-voting member(s) who are identified with industry interests.

20c. How frequent and relevant are the Committee Meetings?

The committee met two times during FY-18. During the morning session on November 20, 2017, the committee discussed three bulk drug substances nominated for inclusion on the list of bulk drug substances that can be used to compound drug products in accordance with section 503A of the FD&C Act: astragalus, L-citrulline, and pregnenolone. During the afternoon session on November 20, 2017, the committee discussed three additional bulk drug substances nominated for inclusion on the list of bulk drug substances that can be used to compound drug products in accordance with section 503A of the FD&C Act: 7-keto dehydroepiandrosterone (7-keto DHEA), epigallocatechin gallate (EGCg), and resveratrol. The majority of the committee (12 members) agreed that L-citrulline should be

included on the 503A Bulks List. The panel commented that the substance is stable, well characterized, and has a long history of use. One committee member was not present for the vote. The committee was split (6 to 5) on whether pregnenolone should be included on the 503A list. The panel expressed concerns with long term use safety signal, lack of evidence of effectiveness for the nominated uses, and the drug's oral availability as a dietary supplement that consumers can take without medical advice, while some members supported its use with pharmacist dispensing and physician supervision on an individual basis for difficult to treat situations. A majority of the committee (9 to 2) agreed that 7-keto dehydroepiandrosterone should not be included on the 503A list. The panel expressed concerns with a lack of evidence to demonstrate efficacy, its long-term safety, and difficulty in formulating the drug substance. The 2 members commented that they did not see a significant negative safety profile and did not see a reason to limit access to patients. During the afternoon session on November 20, 2017, the committee discussed three additional bulk drug substances nominated for inclusion on the list of bulk drug substances that can be used to compound drug products in accordance with section 503A of the FD&C Act: astragalus extract 10:1, epigallocatechin gallate (EGCg), and resveratrol. The committee unanimously (13 members) agreed that astragalus should not be included on the 503A list. The panel expressed concerns with safety, lack of efficacy, and poor characterization of the formulation. The committee unanimously (13 members) agreed that EGCg should not be included on the 503A list. The panel expressed concern with the stability of the drug substance, lack of human data, impurities of the substance, and a lack of efficacy in most of the indications for which it was used. The committee unanimously (12 members) agreed that resveratrol should not be included on the 503A list. The panel expressed concerns with insufficient human clinical studies, issues with safety, and adverse drug interactions. On November 21, 2017, the committee discussed the following drug products, which were nominated as drug products that present demonstrable difficulties for compounding and that cannot be compounded under sections 503A and 503B of the FD&C Act: liposome drug products and drug products produced using hot melt extrusion. A majority of the committee (9 to 1) agreed that liposome drug products should be included on the Difficult to Compound (DTC) List under sections 503A and 503B of the FD&C Act. The panel commented on the complexity of the formulation, drug delivery, and lack of technology available to test these drug products but did note that these products' placement on the DTC List should be reviewed as technology advances in the future. A majority of the committee (7 to 2) agreed that drug products produced using hot melt extrusion should be included on the DTC List under sections 503A and 503B of the FD&C Act. The panel members voting "YES" commented on the complexity of the systems, the need for in vivo testing, and the uncertain bioavailability of the drugs produced using HME. Members voting "NO" commented that prohibiting all HME is premature. Agency Action: The Agency is currently evaluating recommendations

made during the advisory committee meeting. On September 12, 2018, the committee received information on the following two issues to follow up on discussions from previous PCAC meetings: balancing the criteria for the 503A bulk drug substance evaluation and compounding as it relates to dietary supplements. In addition, the committee discussed five bulk drug substances nominated for inclusion on the 503A Bulks List. FDA discussed the following nominated bulk drug substances: Alpha lipoic acid, coenzyme Q10, creatine monohydrate, pyridoxal 5 phosphate, and quercetin dihydrate. The committee unanimously (16 members) agreed that alpha lipoic acid (ALA) solid oral dosage forms should be included on the 503A Bulks List. Many were compelled by the positive data presented about ALA's usage in diabetic neuropathy. The committee unanimously (16 members) agreed that coenzyme Q10 (ubiquinone) for oral administration be included on the 503A Bulks List. The committee members stated that there was a place in therapy for treating mitochondrial disorders and thus coenzyme Q10 helped many patients suffering from these disorders. The committee unanimously (16 members) agreed that creatine monohydrate solid oral dosage forms be included on the 503A Bulks List. Most committee members acknowledged that although the evidence presented was weak and there is risk of renal injury, the substance still suggested some benefit to a patient population that has no effective therapy for their disorder. The committee unanimously (13 members) agreed that pyridoxal 5 phosphate monohydrate (intravenous and oral dosage forms) be included on the 503A Bulks List. The committee stated that pyridoxal 5 phosphate clearly has a life or death benefit for a rare disease. The committee also commented that the substance is well characterized and well supported with efficacy and safety data. The committee unanimously (11 members) agreed that quercetin dihydrate NOT be included on the 503A Bulks List. Many committee members expressed concerns with the lack of reasonable data supporting the use of quercetin dehydrate in its proposed indications, the amount of known drug interactions with this product, and the number of products that are currently available for these conditions that are already proven to be safe and efficacious. Agency Action: The Agency is currently evaluating recommendations made during the advisory committee meeting. It is expected that the committee will meet two to four times during FY-19.

20d. Why can't the advice or information this committee provides be obtained elsewhere?

Members of the committee are drawn from academia, research and/or clinical practice. Their advice and input lends credibility to regulatory decisions made by the agency. The alternate means of obtaining this advice would be to hire large numbers of scientists on a full time basis at great expense to the government.

20e. Why is it necessary to close and/or partially closed committee meetings?

The committee held no closed meetings during the first quarter of FY-18.

21. Remarks

There were no reports required for this committee.

Designated Federal Officer

Cindy Chee Designated Federal Officer

Committee Members	Start	End	Occupation	Member Designation
Bogner, Robin	01/31/2017	09/30/2020	Professor, Univ of Connecticut	Special Government Employee (SGE) Member
Braunstein, Ned	11/13/2014	10/31/2019	Senior Vice President and Head of Regulatory Affairs, Regeneron Pharmaceuticals, Inc.	Representative Member
Carome, Michael	11/24/2014	09/30/2018	CONSUMER REPRESENTATIVE Director, Health Research Group	Special Government Employee (SGE) Member
Davidson, Gigi	11/13/2014	09/30/2018	Director, Clinical Pharmacy Services, North Carolina State University College of Veterinary Medicine	Representative Member
Desai, Seemal	10/01/2017	09/30/2021	President and Medical Director, Innovative Dermatology	Special Government Employee (SGE) Member
Gulur, Padma	11/13/2014	09/30/2020	Vice Chair, Duke University School of Medicine	Special Government Employee (SGE) Member
Hoag, Stephen	11/13/2014	09/30/2020	Professor, University Of Maryland, Baltimore	Special Government Employee (SGE) Member
Humphrey, William	11/13/2014	09/30/2020	Director, Pharmacy Operations, St. Jude Children's Research Hospital	Special Government Employee (SGE) Member
Jungman, Elizabeth	11/14/2017	09/30/2021	Director, The Pew Charitable Trusts	Special Government Employee (SGE) Member
Mixon, William	11/24/2014	10/31/2019	Former Owner, The Compounding Pharmacy	Representative Member
Patel, Kuldip	09/21/2017	09/30/2020	Associate Chief Pharmacy Officer, Duke University Hospital	Special Government Employee (SGE) Member
Vaida, Allen	11/13/2014	09/30/2019	Executive Vice President, Institute for Safe Medication Practices	Special Government Employee (SGE) Member
Venitz, Jurgen	11/13/2014	09/30/2018	Associate Professor, Virginia Commonwealth University School of Pharmacy	Special Government Employee (SGE) Member
Wall, Donna	11/13/2014	09/30/2018	Clincial Pharmacist, Indiana University Hospital	Representative Member

Number of Committee Members Listed: 14

Narrative Description

FDA's strategic priorities in responding to the public health challenges of the 21st century are to advance regulatory science and innovation; strengthen the safety and integrity of the global supply chain; strengthen compliance and enforcement activities to support public health; expand efforts to meet the needs of special populations; advance medical countermeasures and emergency preparedness; advance food safety and nutrition; promote public health by advancing the safety and effectiveness of medical products; establish an effective tobacco regulation, prevention, and control program; and manage for organizational excellence and accountability. The Committee shall provide advice on scientific, technical, and medical issues concerning drug compounding under sections

503A and 503B of the Federal Food, Drug, and Cosmetic Act, and, as required, any other product for which the Food and Drug Administration has regulatory responsibility, and make appropriate recommendations to the Commissioner of Food and Drugs. This supports the development of safe and effective new medical technologies, and advances the status of the Agency as a science-based and science-led regulatory agency, providing global leadership in the protection of public health.

What are the most significant program outcomes associated with this committee?

	Checked if Applies
Improvements to health or safety	✓
Trust in government	✓
Major policy changes	✓
Advance in scientific research	✓
Effective grant making	
Improved service delivery	
Increased customer satisfaction	✓
Implementation of laws or regulatory requirements	✓
Other	

Outcome Comments

NA

What are the cost savings associated with this committee?

	Checked if Applies
None	
Unable to Determine	✓
Under $100,000	
$100,000 - $500,000	
$500,001 - $1,000,000	
$1,000,001 - $5,000,000	
$5,000,001 - $10,000,000	
Over $10,000,000	
Cost Savings Other	

Cost Savings Comments

The utilization of the Pharmacy Compounding Advisory Committee enabled the Agency to obtain required and frequently scarce professional services from medical and scientific experts not otherwise available to the Agency; and to obtain the services of these experts only on an as needed basis rather than on a full time basis. The service of the Committee

resulted in advice for the improvement of the public health, for which it is difficult to assign a financial value.

What is the approximate Number of recommendations produced by this committee for the life of the committee?
81

Number of Recommendations Comments
The committee made 81 recommendations from FY-12 through FY-18. The committee was re-established in FY-12. See question 20a of the annual report for specific accomplishments.

What is the approximate Percentage of these recommendations that have been or will be Fully implemented by the agency?
79%

% of Recommendations Fully Implemented Comments
The function of an advisory committee is purely advisory in nature. Although the FDA most often accepts the recommendations from its committees, the advice is purely advisory in nature, and therefore, the Agency has the option of not implementing the advice.

What is the approximate Percentage of these recommendations that have been or will be Partially implemented by the agency?
10%

% of Recommendations Partially Implemented Comments
The function of an advisory committee is purely advisory in nature. Although the FDA most often accepts the recommendations from its committees, the advice is purely advisory in nature, and therefore, the Agency has the option of not implementing the advice.

Does the agency provide the committee with feedback regarding actions taken to implement recommendations or advice offered?
Yes ☑ No ☐ Not Applicable ☐

Agency Feedback Comments
It usually does. Product approval issues are first released to the sponsor. When appropriate, information is made available to the public. Actions related to guidance

documents or other general matters issues are available publicly when implemented.

What other actions has the agency taken as a result of the committee's advice or recommendation?

	Checked if Applies
Reorganized Priorities	✓
Reallocated resources	
Issued new regulation	✓
Proposed legislation	
Approved grants or other payments	
Other	✓

Action Comments

FDA approves or chooses not to approve an investigational new medical product.

Is the Committee engaged in the review of applications for grants?

No

Grant Review Comments

NA

How is access provided to the information for the Committee's documentation?

	Checked if Applies
Contact DFO	✓
Online Agency Web Site	✓
Online Committee Web Site	✓
Online GSA FACA Web Site	✓
Publications	✓
Other	

Access Comments

NA